Amendments to the Claims

Prior to substantive examination, Applicants have amended claims 17 and 22-35 without any intention of disclaiming equivalents thereof, cancelled claims 1 and 36-38 without prejudice to their subsequent reintroduction into this application or their introduction into a related application, and introduced new claims 39 and 40. The following list of claims replaces all prior versions and lists of claims in the application.

What is claimed is:

1-16. (canceled)

17. (currently amended) A GHRH analogue or a pharmaceutically acceptable salt thereof able to stimulate secretion or synthesis of growth hormone in a mammal, said GHRH analogue ~~analog~~ or pharmaceutically acceptable salt having an *in vitro* potency index substantially higher than the *in vitro* potency index of a native hGHRH1-29 and having formula Tyr- D-Ala^{2}-Asp-Ala-Ile-Phe-Thr-Asn- Ser-D-Tyr^{10}-Arg-Lys-Val-Leu- D-Ala^{15}-Gln-Leu-Ser-Ala-Arg-Lys-Lys^{22}-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2, wherein A30 is a bond or any amino acid sequence of 1 up to 15 residues (SEQ ID NO: 66).

18. (previously presented) A GHRH analogue according to claim 17, wherein the *in vitro* potency index is at least 500-fold higher than the *in vitro* potency index of a native hGHRH1-29.

19. (previously presented) The GHRH analogue of claim 18, wherein the *in vitro* potency index is at least 1500-fold higher than the *in vitro* potency index of a native hGHRH1-29.

20. (previously presented) The GHRH analogue of claim 19, wherein the *in vitro* potency index is at least 2500-fold higher than the *in vitro* potency index of a native hGHRH1-29.

21. (previously presented) The GHRH analogue of claim 17, wherein said GHRH analogue has the formula Tyr- D-Ala^{2}-Asp-Ala-Ile-Phe-Thr-Asn- Ser-D-Tyr^{10}-Arg-Lys-Val-Leu- D-Ala^{15}-Gln-Leu-Ser-Ala-Arg-Lys-Lys^{22}-Leu-Gln-Asp-Ile-Met-Ser-Arg -NH_2.

22. (currently amended) A pharmaceutical composition, comprising:

a) an effective amount of a GHRH analogue or a pharmaceutically acceptable salt thereof, said GHRH analogue or salt comprising formula X:Tyr-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-A10-Arg-Lys-Val-Leu-A15-Gln-Leu-Ser-Ala-Arg-Lys-A22-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2, wherein
A2 is Ala or D-Ala;
A8 is Asn, D-Asn or Ala;
A10 is Tyr or D-Tyr;
A15 is Gly, Ala or D-Ala;
A22 is Leu, D-Leu, Lys or Ala; and
A30 is a bond or any amino acid sequence of 1 up to 15 residues (SEQ ID NO: 67) and wherein said analogue comprises at least one of the above amino acid ~~substitution~~ substitutions in comparison with the amino acid sequence of the native form of hGHRH1-29; and[[;]]

b) a pharmaceutically acceptable carrier.

23. (currently amended) The pharmaceutical composition of claim 22, wherein said GHRH analogue or salt thereof is selected from the group consisting of~~, and wherein~~:

- A2 is D-Ala, A8 is Ala, A15 is Ala, and A22 is Lys;
- A2 is D-Ala, A10 is D-Tyr, and A22 is Lys~~and~~; and
- A2 is D-Ala, A10 is D-Tyr, A15 is D-Ala, and A22 is Lys.

24. (currently amended) The pharmaceutical composition of ~~claim 23~~ claim 22, wherein A2 is D-Ala, A8 is Asn, A10 is D-Tyr, A15 is D-Ala, A22 is Lys and A30 is a bond.

25. (currently amended) A pharmaceutical composition, comprising:

a) an effective amount of a GHRH analogue or a pharmaceutically acceptable salt thereof said GHRH analogue or salt consisting of formula X:Tyr-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-A10-Arg-Lys-Val-Leu-A15-Gln-Leu-Ser-Ala-Arg-Lys-A22-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2, wherein

A2 is Ala or D-Ala;

A8 is Asn, D-Asn or Ala;

A10 is Tyr or D-Tyr;

A15 is Gly, Ala or D-Ala;

A22 is Leu, D-Leu, Lys or Ala; and

A30 is a bond or any amino acid sequence of 1 up to 15 residues (SEQ ID NO: 67) and wherein said analogue comprises at least one of the above amino acid ~~substitution~~ substitutions in comparison with the amino acid sequence of the native form of hGHRH1-29; and[[;]]

b) a pharmaceutically acceptable carrier.

26. (currently amended) The pharmaceutical composition of claim 25, wherein said GHRH analogue or salt thereof is selected from the group consisting of~~, and wherein~~:

- A2 is D-Ala, A8 is Ala, A15 is Ala, and A22 is Lys;
- A2 is D-Ala, A10 is D-Tyr, and A22 is Lys~~and~~; and
- A2 is D-Ala, A10 is D-Tyr, A15 is D-Ala, and A22 is Lys.

27. (currently amended) The pharmaceutical composition of ~~claim 26~~ claim 25, wherein A2 is D-Ala, A8 is Asn, A10 is D-Tyr, A15 is D-Ala, A22 is Lys and A30 is a bond.

28. (currently amended) A pharmaceutical composition for stimulating secretion or synthesis of growth hormone in a mammal in need thereof, the pharmaceutical composition comprising:

a) an effective amount of a GHRH analogue or a pharmaceutically acceptable salt thereof, said GHRH analogue or salt comprising formula X:Tyr-A2-Asp-Ala-Ile-

Phe-Thr-A8-Ser-A10-Arg-Lys-Val-Leu-A15-Gln-Leu-Ser-Ala-Arg-Lys-A22-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2, wherein

A2 is Ala or D-Ala;

A8 is Asn, D-Asn or Ala;

A10 is Tyr or D-Tyr;

A15 is Gly, Ala or D-Ala;

A22 is Leu, D-Leu, Lys or Ala; and

A30 is a bond or any amino acid sequence of 1 up to 15 residues (SEQ ID NO: 67) and wherein said analogue comprises at least one of the above amino acid ~~substitution~~ substitutions in comparison with the amino acid sequence of the native form of hGHRH1-29~~, and~~; and

b) a pharmaceutically acceptable carrier.

29. (currently amended) The pharmaceutical composition of claim 28, wherein said GHRH analogue or salt thereof is selected from the group consisting of~~, and wherein~~:

- A2 is D-Ala, A8 is Ala, A15 is Ala, and A22 is Lys;
- A2 is D-Ala, A10 is D-Tyr, and A22 is Lys~~and~~; and
- A2 is D-Ala, A10 is D-Tyr, A15 is D-Ala, and A22 is Lys.

30. (currently amended) The pharmaceutical composition of ~~claim 29~~ claim 28, wherein A2 is D-Ala, A8 is Asn, A10 is D-Tyr, A15 is D-Ala, A22 is Lys and A30 is a bond.

31. (currently amended) ~~The use of a GHRH analogue, or a pharmaceutically acceptable salt thereof in the preparation of a pharmaceutical composition for~~ A method for treating a mammal in need of growth hormone synthesis or stimulation ~~stimulating the secretion or synthesis of growth hormone in a mammal in need thereof~~, comprising administering an effective amount of ~~said~~ GHRH analogue ~~analog~~ or pharmaceutically acceptable salt comprising formula X: Tyr-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-A10-Arg-Lys-Val-Leu-A15-Gln-Leu-Ser-Ala-Arg-Lys-A22-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2, wherein

A2 is Ala or D-Ala;

A8 is Asn, D-Asn or Ala;

A10 is Tyr or D-Tyr;

A15 is Gly, Ala or D-Ala;

A22 is Leu, D-Leu, Lys or Ala; and

A30 is a bond or any amino acid sequence of 1 up to 15 residues (SEQ ID NO: 67) and wherein said analogue comprises at least one of the above amino acid ~~substitution~~ substitutions in comparison with the amino acid sequence of the native form of hGHRH1-29.

32. (currently amended) The ~~use~~ method as defined in claim 31, wherein said GHRH analogue or salt thereof is selected from the group consisting of~~, and wherein~~:

- A2 is D-Ala, A8 is Ala, A15 is Ala, and A22 is Lys;
- A2 is D-Ala, A10 is D-Tyr, and A22 is Lys~~and~~; and
- A2 is D-Ala, A10 is D-Tyr, A15 is D-Ala, and A22 is Lys.

33. (currently amended) The ~~use~~ method as defined in ~~claim 32~~ claim 31, wherein A2 is D-Ala, A8 is Asn, A10 is D-Tyr, A15 is D-Ala, A22 is Lys and A30 is a bond.

34. (currently amended) The ~~use~~ method according to claim 31, wherein said mammal has a disorder selected from the group consisting of hypothalamic pituitary dwarfism, burns, osteoporosis, renal failure, non-union bone-fracture, acute/chronic debilitating illness or infection, wound healing, reduction of the incidence of post-surgical problems, lactation failure, infertility in women, cachexia in cancer patients, anabolic and/or catabolic problems, T-cell immunodeficiencies, neurodegenerative conditions, GHRH receptor-dependent tumors, aging, sleep disorders, muscle wasting diseases such as in sarcopenic patients, frail elderlies, HIV patients and cancer patients having radiotherapy and chemotherapy side-effects.

35. (currently amended) The ~~use~~ method according to claim 34, wherein said muscle wasting diseases are selected from the group consisting of[[;]]: sarcopenia, frailty in elderlies, HIV and cancer.

36-38. (canceled)

39. (new) A pharmaceutical composition, comprising:

a) an effective amount of a GHRH analogue or a pharmaceutically acceptable salt thereof, said GHRH analogue or salt comprising formula X:Tyr-A2-Asp-Ala-Ile-Phe-Thr-A8-A9-A10-Arg-Lys-Val-Leu-A15-Gln-Leu-Ser-Ala-Arg-A21-A22-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2, wherein
A2 is Ala or D-Ala;
A8 is Asn, D-Asn or Ala;
A9 is Ala or Ser;
A10 is Tyr or D-Tyr;
A15 is Gly, Ala or D-Ala;
A21 is Lys or D-Lys;
A22 is Leu, D-Leu, Lys or Ala; and
A30 is a bond or any amino acid sequence of 1 up to 15 residues (SEQ ID NO. 65) and wherein said analogue comprises at least one of the above amino acid substitutions in comparison with the amino acid sequence of the native form of hGHRH1-29; and

b) a pharmaceutically acceptable carrier.

40. (new) A method for treating a mammal in need of growth hormone synthesis or stimulation comprising administering an effective amount of GHRH analogue or pharmaceutically acceptable salt comprising formula X:Tyr-A2-Asp-Ala-Ile-Phe-Thr-A8-A9-A10-Arg-Lys-Val-Leu-A15-Gln-Leu-Ser-Ala-Arg-A21-A22-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2, wherein

A2 is Ala or D-Ala;

A8 is Asn, D-Asn or Ala;

A9 is Ala or Ser;

A10 is Tyr or D-Tyr;

A15 is Gly, Ala or D-Ala;

A21 is Lys or D-Lys;

A22 is Leu, D-Leu, Lys or Ala; and

A30 is a bond or any amino acid sequence of 1 up to 15 residues (SEQ ID NO. 65) and wherein said analogue comprises at least one of the above amino acid substitutions in comparison with the amino acid sequence of the native form of hGHRH1-29.